

[Open Peer Review on Qeios](#)

# Autologous CD19-CD8-CD28-CD3zeta-CAR-mbIL15-HER1t T Cells

National Cancer Institute

## Source

National Cancer Institute. *Autologous CD19-CD8-CD28-CD3zeta-CAR-mbIL15-HER1t T Cells*. NCI Thesaurus. Code C150906.

A preparation of autologous, genetically modified T-lymphocytes, that have been electroporated ex vivo with sleeping beauty (SB)-derived DNA plasmids, expressing a second-generation chimeric antigen receptor (CAR) composed of a mouse single-chain variable fragment (scFv) specific for the tumor-associated antigen (TAA) cluster of differentiation 19 (CD19) that is linked to the co-stimulatory molecules T-cell surface glycoproteins CD8 and CD28 and the zeta chain of the T-cell receptor (TCR)/CD3 complex (CD3-zeta) and co-expressed with a chimeric membrane-bound fusion protein comprised of interleukin-15 (IL-15) fused to IL-15 receptor (mbIL15) and a safety/kill switch composed of a truncated form of the human epidermal growth factor receptor (ErbB1t; EGFR) (HER1t), with potential immunostimulating and antineoplastic activities. Upon reintroduction of the autologous CD19-CD8-CD28-CD3zeta-CAR-mbIL15-HER1t T cells into the patient, the T-cells target and bind to CD19-expressing tumor cells, thereby inducing selective toxicity in CD19-expressing tumor cells. CD19 is a B-cell specific cell surface antigen expressed in all B-cell lineage malignancies. HER1t can promote selective elimination of the CAR-T cells through cetuximab-induced antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). IL-15 is a pro-survival cytokine that is required for the maintenance of long-lived CD8+ memory T-cells and use of mbIL15 preserves T stem-cell memory (TSCM) through sustained IL-15 signaling, improves T-cell persistence and potentiates the immune response against tumor cells. The SB system permits electroporation of the CAR, the IL-15 fusion variant and safety switch transgenes into T-cells without the need for viral vectors and accelerates the manufacturing process.